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DATE: Tuesday, October 11, 2005

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☐	L5	L4 and (divergen$ or opposit$)	33
☐	L4	L3 same enhancer	43
☐	L3	l1 or l2	364
☐	L2	bi-direction$ near3 (promoter or regulator$ region or regulat$ element or regulat$ sequence)	108
☐	L1	bidirection$ near3 (promoter or regulator$ region or regulat$ element or regulat$ sequence)	291

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         MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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=> s (bidirection? or bi direction?) (3a) (promoter or regulat? region or regulat?
element or regulat? sequence)
L1        996 (BIDIRECTION? OR BI DIRECTION?) (3A) (PROMOTER OR
REGULAT? REGIO
          N OR REGULAT? ELEMENT OR REGULAT? SEQUENCE)

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L2         77 L1 AND ENHANCER

=> l2 and (divergen? or opposite)
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L3         33 L2 AND (DIVERGEN? OR OPPOSITE)

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L4         20 DUP REM L3 (13 DUPLICATES REMOVED)

=> d bib abs 1-
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L4  ANSWER 1 OF 20  CAPLUS  COPYRIGHT 2005 ACS on STN
AN  2004:934504  CAPLUS
DN  141:406766
TI  Bicistronic lentiviral vectors carrying synthetic bi-directional promoters
    for gene therapy in human
IN  Naldini, Luigi; Amendola, Mario; Vigna, Elisa
PA  Fondazione Centro San Raffaele del Monte Tabor, Italy
SO  PCT Int. Appl., 54 pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.         KIND  DATE       APPLICATION NO.     DATE
    ---------------    ----  --------   ------------------  --------
PI  WO 2004094642      A2    20041104   WO 2004-IT227       20040421
    WO 2004094642      A3    20050512
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
           CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
           GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
           LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
           NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
           TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
           BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
           ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
           SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
           TD, TG
PRAI US 2003-465080P    P   20030424
AB  It is described a ***bidirectional***  ***promoter***  for
    expression of at least two coding sequences in  ***opposite***
    direction in animal cells. A first minimal promoter sequence is derived
    from cytomegalovirus (CMV) or mouse mammary tumor virus (MMTV)
genomes;.
    A full efficient promoter sequence is derives from ubiquitously expressed
    genes comprising the phosphoglycerate kinase or the ubiquitin gene. The
    invention also relates to transformation of brain neurons, umbilical vein
    endothelium, lymphocytes or human hematopoietic cell with bidirectional
    expression cassettes.

L4  ANSWER 2 OF 20  CAPLUS  COPYRIGHT 2005 ACS on STN
AN  2004:233848  CAPLUS
DN  140:315894
TI  Human aldehyde reductase promoter allows simultaneous expression of two
    genes in  ***opposite***  directions
AU  Barski, Oleg A.; Siller-Lopez, Fernando; Bohren, Kurt M.; Gabbay, Kenneth
    H.; Aguilar-Cordova, Estuardo
CS  Baylor College of Medicine, Houston, TX, 77030, USA
SO  BioTechniques (2004), 36(3), 382,384,386,388
    CODEN: BTNQDO; ISSN: 0736-6205
PB  Eaton Publishing Co.
DT  Journal
LA  English
AB  The ability of aldehyde reductase promoter (ARP) to drive expression of
    two genes simultaneously was tested in transient transfections using
    firefly and Renilla luciferase genes as reporters. Both firefly and
    Renilla luciferases were expressed from dual-gene constructs at similar
    levels in cell lines from different tissue origins, including liver,
    fibroblast, and kidney. The reverse orientation of the promoter was
    generally stronger than the forward one in the constructs tested. The
    ratio of promoter orientations, i.e., reverse to forward, for firefly
    luciferase varied between 2- and 3-fold, while the same ratio for Renilla
    luciferase was 5- to 6-fold. The results demonstrate that it is possible
    to achieve the simultaneous expression of two genes with minimal ARP.
    Expression from ARP was comparable in strength to that of a simian virus
    40 promoter/ ***enhancer***  and that of a herpes simplex virus
    thymidine kinase promoter.
RE.CNT  19  THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD
        ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4  ANSWER 3 OF 20  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation
on STN
    DUPLICATE 1
AN  2004:455608  BIOSIS
DN  PREV200400453279
TI  A  ***bi***  -  ***directional***  ***promoter***  at the upstream of
    pp38 gene from Marek's disease virus.
AU  Ding Jia-bo; Cui Zhi-zhong [Reprint Author]; Sun Shu-hong; Jiang Shi-jin
CS  Coll Anim Sci, Shandong Agr Univ, Taian, 271018, China
    zzcui@sdau.edu.cn
SO  Weishengwu Xuebao, (April 2004) Vol. 44, No. 2, pp. 162-166. print.
    CODEN: WSHPA8. ISSN: 0001-6209.
DT  Article
LA  Chinese
ED  Entered STN: 24 Nov 2004
    Last Updated on STN: 24 Nov 2004
AB  Marek's disease virus (MDV)'s replicating origin is at the upstream of
    pp38 gene. On both sides of the region, there are several conserved
    promoter motifs such as TATA-box, CAAT-box, etc, which is regarded as a
```

bi - ***directional*** ***promoter*** and ***enhancer*** . In order to validate the ***divergent*** promoting activity in vivtro, we cloned MDV pp38 gene open reading frame (ORF) into pUC18 vector, and constructed pUC-pp38 as a basic plasmid. The 789bp PCR fragment which contains the complete sequences of MDV's replicating origin was cloned at the upstream of pp38 gene in pUC-pp38 at two different directions. The positive clones named as pProfpp38 and pProrpp38 were transfected into chicken embryo fibroblast (CEF) cells. 24 hours after the transfection, green fluorescence can been seen on the cytoplasm of CEF in immunofluorecent assay (IFA). 48 hours and on after the transfection, the IFA positive cells will be up to 50% and the expression level can be maintained for a few days. The results show that this region has bi-directional promoting activity. 320bp was confirmed as the core sequence of this promoter with PCR technique.

L4 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:350563 CAPLUS
DN 141:83181
TI Bi-directional duplex promoters with duplicated enhancers significantly increase transgene expression in grape and tobacco
AU Li, Zhijian T.; Jayasankar, Subramamnian; Gray, D. J.
CS Institute of Food and Agricultural Sciences, Mid-Florida Research and Education Center, University of Florida, Apopka, FL, 32703-8504, USA
SO Transgenic Research (2004), 13(2), 143-154
CODEN: TRSEES; ISSN: 0962-8819
PB Kluwer Academic Publishers
DT Journal
LA English
AB Novel bi-directional duplex promoters (BDDP) were constructed by placing two identical core promoters ***divergently*** on both upstream and downstream sides of their duplicated ***enhancer*** elements. Ests. of promoter function were obtained by creating versions of CaMV 35S and CsVMV BDDPs that contained reporter marker genes encoding .beta.-glucuronidase (GUS) and enhanced green fluorescent protein (EGFP) interchangeably linked either to the upstream or downstream core promoters. GUS was used for quant. anal. of promoter function, whereas, EGFP allowed visual qual. evaluation. In addn., the GUS and EGFP genes placed in downstream positions were modified by translational fusion with neomycin phosphotransferase (NPTII) to allow simultaneous monitoring of promoter activity and selection of stable transformants. These versions of BDDP were compared with each other and with equiv. unidirectional constructs by evaluating their expression in grape somatic embryos (SE), BDDP exhibited transient GUS expression 206- and 300-fold greater in downstream and upstream configurations, resp., compared to a unidirectional 35S core promoter. Compared with a unidirectional double enhanced 35S promoter, BDDPs exhibited 0.5- and 3-fold increased GUS expression from downstream and upstream core promoters, resp. The same differences in expression levels detd. quant. with GUS were distinguished qual. with EGFP. Constructs using CsVMV core promoters yielded results relative to those obtained with 35S promoter. For example, the upstream BDDP CsVMV core promoter provided a 200-fold increase in GUS expression compared to a unidirectional core promoter. However, CsVMV promoter was found to have higher promoter activity than 35S promoter in both BDDP and unidirectional constructs. Incorporation of an addnl. duplicated ***enhancer*** element to BDDPs resulted in increased expression. For example, a 35S BDDP with two ***divergently*** arranged duplicated ***enhancer*** elements resulted in over a 6-fold increase in GUS expression in stably transformed tobacco plants compared to a BDDP with one duplicated ***enhancer*** element. Data demonstrate that BDDP composed of ***divergently*** -arranged core promoters sepd. by duplicated enhancers, all derived from a single promoter sequence, can be used to significantly enhance transgene expression and to direct synchronized expression of multiple transgenes.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:637849 CAPLUS
DN 137:180785
TI A ***bi*** - ***directional*** dual ***promoter*** complex with enhanced promoter activity for transgene expression in eukaryotes
IN Li, Zhijian; Gray, Dennis J.
PA University of Florida, USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002064804	A2	20020822	WO 2002-US4188	20020213
WO 2002064804	A3	20030417		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2443266	AA	20020822	CA 2002-2443266	20020213
EP 1360310	A2	20031112	EP 2002-718955	20020213

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2005188432	A1	20050825	US 2002-75105	20020213
BR 2003003417	A	20050510	BR 2003-3417	20030821
PRAI US 2001-268358P	P	20010213		
WO 2002-US4188	W	20020213		

AB The present invention is directed to ***bidirectional*** ***promoter*** complexes that are effective for enhancing transcriptional activity of transgenes. The bidirectional promoters of the invention include a modified ***enhancer*** region with at least two core promoters on either side of the modified ***enhancer*** in a ***divergent*** orientation. The enhanced promoter activities are demonstrated using a construct contg. two reporter genes (directed by the same ***enhancer*** -core promoter element in the tandem order) by reverting the 2nd promoter orientation in the ***divergent*** direction and keeping two copies of ***enhancer*** -core promoter elements back to back. These two back-to-back ***enhancer*** -core ***promoter*** elements, also called ***bi*** - ***directional*** dual ***promoter*** complex BDPC, are tested in the contact of two ***enhancer*** or 4- ***enhancer*** plus CaMV 35S core promoter. The dramatic increase of both reporter genes are obsd. in the transformed grape. Furthermore, various promoter-based BDPC fragments are provided for gene regulation in transgenic plants.

L4 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:810671 CAPLUS
DN 132:133149
TI The bi-directional transcriptional promoters for the latency-relating transcripts of the pp38/pp24 mRNAs and the 1.8 kb-mRNA in the long inverted repeats of Marek's disease virus serotype 1 DNA are regulated by common promoter-specific enhancers
AU Shigekane, H.; Kawaguchi, Y.; Shirakata, M.; Sakaguchi, M.; Hirai, K.
CS Department of Tumor Virology, Division of Virology and Immunology, Medical Research Institute, Tokyo Medical and Dental University, Tokyo, Japan
SO Archives of Virology (1999), 144(10), 1893-1907
CODEN: ARVIDF; ISSN: 0304-8608
PB Springer-Verlag Wien
DT Journal
LA English
AB In cell lines established from Marek's disease tumors, several viral transcripts are expressed and among them the products of pp38/pp24 mRNA and 1.8 kb-mRNA have been suggested to be involved in viral oncogenicity. The long inverted repeats of Marek's Disease virus serotype 1 (MDV 1) genome contain closely located transcriptional promoters for phosphorylated protein pp38/pp24 and 1.8 kb-mRNA. These promoters initiate transcription in ***opposite*** directions and are sepd. only by a short ***enhancer*** region, which is likely to regulate both promoters simultaneously. The authors have analyzed the transcription activity of these promoters in MDV1 (Md5 strain) infected CEF by transient expression of CAT reporter genes and found that the promoters were in fact active in infected cells and the promoter for 1.8 kb-mRNA was more active than the pp38/pp24 promoter. Deletion anal. of the short ***enhancer*** region revealed that the 30 bp region overlapping the ***enhancer*** elements for 1.8 kb-mRNA was important for promoter activity for pp38/pp24. The gel shift anal. revealed that nuclear factor(s) actually bound to the overlapping 30 bp region. In addn., the activity of these promoters in infected cells varied with MDV strains. These results suggest that pp38/pp24 and 1.8 kb-mRNA promoters share a common regulatory sequence but a viral or a cellular factor(s) induced by viral infection regulates the promoter by distinct mechanisms.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 2
AN 2000013364 EMBASE
TI The mannopine synthase promoter contains vectorial cis-regulatory elements that act as enhancers and silencers.
AU Guevara-Garcia A.; Lopez-Bucio J.; Herrera-Estrella L.
CS L. Herrera-Estrella, Dept. Ingenieria Genetica Plantas, Centro Invest. Estud. Avanzados IPN, Unidad Irapuato, Apartado Postal 629, 36500 Irapuato Guanajuato, Mexico. lherrera@irapuato.ira.cinvestav.mx
SO Molecular and General Genetics, (1999) Vol. 262, No. 4-5, pp. 608-617.
Refs: 49
ISSN: 0026-8925 CODEN: MGGEAE
CY Germany
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20000120
Last Updated on STN: 20000120
AB A 479-bp ***bi*** - ***directional*** ***promoter*** controls the expression of two genes (mas1' and mas2') that encode enzymes for the synthesis of the opine mannopine in plant tissues infected with Agrobacterium tumefaciens. This 5' regulatory region (mas promoter) contains all the cis-acting elements involved in mediating the complex regulatory properties of these genes in plants. Using different mas

promoter regions fused to a minimal 35S promoter (35S.DELTA.108), we found that the regulatory properties of these ***divergent*** promoters result from the presence of orientation-dependent negative and positive regulatory regions. Some of these elements have the unusual property of acting as enhancers in one orientation and as silencers in the other. Using electrophoretic mobility shift analysis (EMSA), we showed that the functional mas promoter regions identified by fluorometric and histochemical assays for reporter gene activity in transgenic plants have the ability specifically to bind nuclear protein factors from Nicotiana tabacum, Phaseolus vulgaris, Solanum tuberosum, and Arabidopsis thaliana.

L4 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:25851 CAPLUS
DN 132:176261
TI Analysis of ***bi*** - ***directional*** ***promoter*** - ***enhancer*** region located in BamHI-H fragment of Marek's disease virus serotype 1
AU Shigekane, Hironori
CS Dep. Tumor Virol., Div. Virol. Immunol., Med. Res. Inst., Tokyo Med. Dent. Univ., Yushima 1-5-45, Bunkyo-ku, Tokyo, 113-8510, Japan
SO Kachiku Seikagaku (1999), 36(1), 15-27
CODEN: KCSIE6; ISSN: 1340-5535
PB Kachiku Seikagakkai
DT Journal; General Review
LA Japanese
AB A review with 49 refs. Marek's disease virus serotype 1 (MDV1), a chicken alphaherpesvirus, causes malignant lymphomas (T4 cells) and neurol. disorders. In the 1970's, vaccine has been developed and is still the only com. vaccine for oncogenic virus until today, although it cannot prevent the disease completely. Many viral encoded proteins have been investigated to study the function of tumorigenicity of this virus, but still, little is known at present. In this paper, the author focused on BamHI-H fragment of very virulent strain (Md5) of MDV1, which encodes two viral proteins, a phosphorylated protein pp38 and 1.8 kb-mRNA, resp. The two proteins transcript in ***opposite*** directions, flanked by only about 300-bp region. This region seems to have promoter and ***enhancer*** elements by sequence analyze. The author has revealed for the first time that this region functions as promoter for both directions, although the promoter for 1.8 kb-mRNA was more active than pp38 promoter. Deletion anal. of this region revealed that 30 bp-region overlapping the ***enhancer*** element for 1.8 kb-mRNA was also important for activity for pps8. Further, this 30 bp overlapping region was also well conserved in the promoter region of pp38 homologues of avirulent MDV strains. In addn., pp38 homologues were found in ORF73 of Kaposi's Sarcoma-assocd. herpesvirus (KSHV) and Herpesvirus Saimili. ORF73 of KSV is now known as a component of latency-assocd. nuclear antigen (LNA), although the function of LNA is not known at present. Finally, the author will discuss briefly about other viral proteins related to pp38 and 1.8 kb-mRNA of MDV1.

L4 ANSWER 9 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 3
AN 1998274901 EMBASE
TI Evidence for a ***bidirectional*** ***promoter*** complex within the X gene of woodchuck hepatitis virus.
AU Shimoda A.; Sugata F.; Chen H.-S.; Miller R.H.; Purcell R.H.
CS R.H. Miller, Hepatitis Viruses Section, Laboratory of Infectious Diseases, Nat. Inst. Allergy/Infect. Diseases, Bethesda, MD 20892, United States
SO Virus Research, (1998) Vol. 56, No. 1, pp. 25-39.
Refs: 69
ISSN: 0168-1702 CODEN: VIREDF
PUI S 0168-1702(98)00050-1
CY Netherlands
DT Journal; Article
FS 004 Microbiology
LA English
SL English
ED Entered STN: 19980904
Last Updated on STN: 19980904
AB The genetic organization of hepadnaviruses is unusual in that all cis-acting regulatory sequences are located within genes. Thus, in the mammalian hepadnavirus genome, the presurface, surface, and X transcript promoters reside within the polymerase gene while the pregenome transcript promoter is located within the X gene. In this study we have identified two additional promoters within the woodchuck hepatitis virus (WHV) X gene that stimulate production of transcripts in vitro. First, we cloned regions of the WHV X gene into a promoterless expression vector (pGL2) to examine their ability to promote expression of firefly luciferase and mapped a previously unidentified promoter to positions 1475-1625 of the WHV8 genome. Deletion analysis revealed that the essential domain of this promoter, termed the ORF5/.DELTA.X transcript promoter, mapped to nucleotides 1525-1625. Analysis revealed that this transcript initiated at nucleotide 1572 in both human (HuH-7) and woodchuck (WLC-3) hepatoma cell lines. Consistent with this finding, DNA footprinting analysis revealed protection of nucleotides 1567-1578 on the positive strand of the WHV8 genome. The function of this transcript in vivo is unclear, however, it may be used to produce a truncated form of the X protein that initiates at an AUG codon at position 1743-1745 on the WHV8 genome. Next, a second promoter was identified at positions 1625-1975 that was responsible for production of an antisense transcript. The activity of this promoter was comparable to that of the previously characterized surface transcript promoter of WHV in the absence of an ***enhancer*** . The antisense transcript promoter resides immediately upstream of open reading frame (ORF) 6, a previously identified ORF on the strand ***opposite*** of the known WHV protein-encoding sequences, that is thought to represent a vestigial gene. Analysis indicates that the antisense transcript had multiple start sites: nucleotides 1683 and 1762 on the WHV8 genome when assayed in HuH-7 cells, and nucleotide 1786 when assayed in WLC-3 cells. These data are consistent with footprinting analysis of supercoiled WHV DNA that revealed that the regions encompassing nucleotides 1696-1685, 1781-1766, and 1801-1787 on the negative sense DNA strand were protected from nuclease degradation. It is possible that such a transcript was once used in protein expression in an ancestral virus and may now be used for genetic control of WHV replication and/or gene expression. Overall, these data are consistent with the presence of a ***bidirectional*** ***promoter*** complex within the WHV X gene. Copyright (C) 1998 Published by Elsevier Science B.V.

L4 ANSWER 10 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 95105499 EMBASE
DN 1995105499
TI Coordinate regulation of the human TAP1 and LMP2 genes from a shared ***bidirectional*** ***promoter*** .
AU Wright K.L.; White L.C.; Kelly A.; Beck S.; Trowsdale J.; Ting J.P.-Y.
CS Dept. of Microbiology-Immunology, UNCL Comprehensive Cancer Center, University of North Carolina,Chapel Hill, NC 27599, United States
SO Journal of Experimental Medicine, (1995) Vol. 181, No. 4, pp. 1459-1471.
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 950503
Last Updated on STN: 950503
AB Recently, four genes (TAP1, TAP2, LMP2, LMP7) involved or potentially involved in the processing and transport of major histocompatibility complex class I-associated antigen to the endoplasmic reticulum have been identified. We now report the initial characterization of the ***bidirectional*** ***promoter*** for the human transporter associated with antigen processing 1 (TAP1) and low molecular mass polypeptide 2 (LMP2) genes. These genes are ***divergently*** transcribed from a central promoter region of only 593 bp. Functional analysis using a bidirectional reporter system demonstrates the minimal 593- bp promoter is sufficient for concurrent expression in both directions. There is no TATA box homology at either end but there is a prevalence of GC boxes. Transcription is initiated at multiple sites for each gene without any of the TAP1 transcripts overlapping with the LMP2 transcripts. The region proximal to the TAP1 gene is required for maximal basal level expression of not only TAP1 but also LMP2. Furthermore, this region is necessary for tumor necrosis factor .alpha. (TNF-.alpha.) induction of both genes. Site-specific mutations of an NF- .kappa.B element in the TAP1 proximal region blocked induction by TNF-.alpha. in both the TAP1 and LMP2 directions. An adjacent GC box was required for basal expression of both genes as well as augmenting the TNF-.alpha. induction of the distal LMP2 gene. In vivo genomic foot-printing of this region revealed strong protein/DNA interactions at the NF-.kappa.B and GC box consensus sequences. In vitro binding studies confirmed the capacity of the NF-.kappa.B site to bind p50/p65 and p52/p65 heterodimers and of the GC box to bind Sp1. Thus, the promoter elements proximal to the TAP1 gene play a significant role in regulating basal and induced expression of both TAP1 and LMP2. The findings presented in this report clearly link LMP2 expression with TAP1 expression and provide additional suggestive evidence linking LMP2 to class I antigen presentation.

L4 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:540787 CAPLUS
DN 123:190382
TI CpG methylation has differential effects on the binding of YY1 and ETS proteins to the ***bi*** - ***directional*** ***promoter*** of the Surf-1 and Surf-2 genes
AU Gaston, Kevin; Fried, Mike
CS Dep. Biochem., Sch. Med. Sci., Univ. Bristol, Bristol, BS8 1TD, UK
SO Nucleic Acids Research (1995), 23(6), 901-9
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The ***divergently*** transcribed Surf-1 and Surf-2 housekeeping genes are sepd. by a ***bi*** - ***directional*** , TATA-less ***promoter*** which lies within a CpG-rich island. Here we show that CpG methylation severely reduces transcription in the direction of both Surf-1 and Surf-2. Previous work has identified three promoter elements (Su1, Su2 and Su3) which are conserved between the human and mouse Surf-1/Surf-2 promoters. These elements bind transcription factors present in human and mouse cell nuclear exts. in vitro and mutations which prevent factor binding also reduce promoter activity in vivo. Transcription initiation factor YY1 binds to the Su1 site and stimulates transcription in the direction of Surf-1 and, to a lesser extent, Surf-2. Here we show that members of the ETS family of transcription factors bind to the Su2 site. Although the Su1 factor binding site contains three CpG dinucleotides, the binding of YY1 is not affected by CpG methylation. In contrast, CpG methylation abolishes the binding of ETS proteins to the Su2

site; methylation of a single cytosine, at position 3 of the consensus ETS site, is sufficient to prevent factor binding. This direct effect on the binding of ETS proteins is, however, not in itself sufficient to explain the repression of this promoter by CpG methylation. A mutation of the Su2 site which removes the sequence CpG, but which does not prevent ETS factor binding, fails to relieve this promoter from repression by CpG methylation.

L4 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:680046 CAPLUS
DN 123:248352
TI CpG methylation and the binding of YY1 and ETS proteins to the Surf-1/Surf-2 ***bidirectional*** ***promoter***
AU Gaston, Kevin; Fried, Mike
CS Department of Biochemistry, University of Bristol, Bristol, BS8 1TD, UK
SO Gene (1995), 157(1/2), 257-9
CODEN: GENED6; ISSN: 0378-1119
PB Elsevier
DT Journal
LA English
AB The ***divergently*** transcribed Surf-1 and Surf-2 genes are sepd. by a ***bi*** - ***directional*** , TATA-less ***promoter*** which contains 3 important factor-binding sites, Su1, Su2 and Su3. The transcription initiation factor YY1 binds to the Su1 site and stimulates transcription in the direction of Surf-1 and, to a lesser extent, Surf-2. Members of the ETS family of transcription factors bind to the Su2 and Su3 sites. Also, in transient transfection assays, transcription in both the Surf-1 and the Surf-2 direction is severely reduced by CpG methylation. Although the Su1 site contains three CpG dinucleotides, the binding of YY1 is not affected by CpG methylation. In contrast, the binding of two ETS factors (ETS-2 and PEA-3) to the Su2 site (which also contains three CpG dinucleotides) is totally abolished by CpG methylation. Finally, methylation of a single C within the Su2 site is sufficient to prevent ETS factor binding.

L4 ANSWER 13 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 4
AN 92029624 EMBASE
DN 1992029624
TI Functional analysis of cis-elements, auxin response and early developmental profiles of the mannopine synthase ***bidirectional*** ***promoter*** .
AU Leung J.; Fukuda H.; Wing D.; Schell J.; Masterson R.
CS Max-Planck-Institut, fur Zuchtungsforschung, Carl-von-Linne-Weg 10,W-5000 Koln 30, Germany
SO Molecular and General Genetics, (1991) Vol. 230, No. 3, pp. 463-474.
ISSN: 0026-8925 CODEN: MGGEAE
CY Germany
DT Journal; Article
FS 004 Microbiology
022 Human Genetics
LA English
SL English
ED Entered STN: 920320
Last Updated on STN: 920320
AB The dual MAS1'-2' promoter regulating two ***divergently*** transcribed mannopine synthase genes has been widely employed in plant expression vectors. As part of an effort towards its rational design as a genetic engineering tool, we have undertaken a functional analysis of the promoter by deletion mutagenesis and by the use of hybrid promoter constructs. Our results indicate that the central region of the intergenic promoter is composed of at least four domains. Three of these contain complementary sequences, which can potentially hybridize to form alternative palindromic structures. These three domains can function cooperatively, and in an orientation-independent manner, in imparting a sevenfold higher expression level at the 2' end relative to the corresponding 1'. The remaining domain is characterized by tracts of repeated A/T-rich elements, and appears to confer the weak activity at the MAS1' promoter end. However, even though this A/T-rich DNA segment is functional, our deletion analysis provided strong evidence that it is completely dispensable for wild-type promoter activity. In addition, the relative distances between these ***enhancer*** domains and the 1'-2' TATA-proximal regions can have a pronounced influence on the level of expression in both directions. In young tobacco seedlings, the two promoter ends are expressed in similar, if not identical, tissues in the aerial parts of the plants, but major differences can be observed in roots. Transient expression assays using hybrid promoter constructs showed that cis-elements that can respond to auxin induction signals are redundant in nature, in that they are dispersed throughout the promoter and showed no obvious consensus sequence.

L4 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1990:546325 CAPLUS
DN 113:146325
TI Regulation of ***divergent*** transcription of the genes coding for basement membrane type IV collagen
AU Pollner, R.; Fischer, G.; Poeschl, E.; Kuehn, K.
CS Abt. Bindegewebsforsch., Max Planck Inst. Biochem., Martinsried, D-8033, Germany
SO Annals of the New York Academy of Sciences (1990), 580(Struct., Mol. Biol., Pathol. Collagen), 44-54
CODEN: ANYAA9; ISSN: 0077-8923
DT Journal
LA English
AB The genes coding for the 2 polypeptide chains, .alpha.1(IV) and .alpha.2 (IV), of type IV collagen are very closely linked, transcribed in ***opposite*** directions, and use a common and ***bidirectional*** ***promoter*** with a length of 127 bp. In accordance with the symmetry of the promoter itself, a sym. organization of sequence motifs (SP1, CCAAT) was also obsd. in flanking regions. Specific binding of nuclear factors to the promoter and flanking regions was detected, which indicates their involvement in transcriptional activation. This suggests that the symmetry of the type IV collagen promoter and its flanking regions may be a prerequisite for its bidirectional function. In transient gene expression systems no significant activity of the type IV collagen promoter was obsd. in either direction. This implies that addnl. enhancing elements are essential for the efficient and tissue-specific transcription of both type IV collagen genes. Screening for such controlling elements within the .alpha.1(IV) and the .alpha.2(IV) gene demonstrated that transcription in the direction of the .alpha.2(IV) gene is activated by an element located in the first intron of the .alpha.2 gene. Its enhancing effect is strictly dependent on the intact structure of this region. Alteration of orientation and distance to the promoter destroys its activity completely. This element, located about 100-600 bp downstream from the start site of .alpha.2(IV) transcription, apparently functions synergistically with the common promoter, to activate transcription in the .alpha.2 direction. No addnl. enhancing elements were found in either gene. Explanations for the discrepancy with previous data, which define an enhancing element within the first intron of the .alpha.1(IV) gene of mouse, are only speculative at present.

L4 ANSWER 15 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 5
AN 1989:474255 BIOSIS
DN PREV198988110015; BA88:110015
TI C-HA-RAS GENE ***BIDIRECTIONAL*** ***PROMOTER*** EXPRESSED IN-VITRO LOCATION AND REGULATION.
AU LOWNDES N F [Reprint author]; PAUL J; WU J; ALLAN M
CS DEP GENETICS MED, COLL PHYSICIANS AND SURG COLUMBIA UNIV, 630 WEST 168TH ST, NEW YORK, NEW YORK 10032, USA
SO Molecular and Cellular Biology, (1989) Vol. 9, No. 9, pp. 3758-3770.
CODEN: MCEBD4. ISSN: 0270-7306.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 17 Oct 1989
Last Updated on STN: 17 Oct 1989
AB Increased transcriptional activity of the c-Ha-ras gene product is correlated with induction of several important human tumor types. For this reason, we have investigated the nature of the c-Ha-ras promoter and the factors that regulate its expression. Using S1 and primer extension analysis of c-Ha-ras RNA from EJ cells, we have identified 18 initiation sites within an upstream exon (exon-1) whose 3' end (the donor splice site [D]) is located 1,105 base pairs (bp) upstream of the ATG codon. The furthest-upstream initiation site is located -191 bp relative to D, and the furthest downstream is located -16 bp relative to D. Transient expression assays, in which a series of mutants spanning this region were ligated to a promoterless chloramphenicol acetyltransferase vector, functionally confirmed the position and extent of this promoter. Mutational analysis further located a 47-bp element located between -243 and -196 relative to D that up-regulated transcriptional activity of the promoter region by 20- to 40-fold. This region contained both a GC box known to bind SP1 and a CCAAT box. Insertion of a simian virus 40 ***enhancer*** 5' to the promoter up-regulated transcription from each initiation site by approximately 10- to 20-fold. We have also localized, both by chloramphenicol acetyltransferase assay and by S1 analysis, a strong promoter operating in the direction ***opposite*** that of the gene and originating immediately 5' to the 47-bp regulatory region. The reverse promoter was found to have nine initiation sites between -248 and -278 relative to D.

L4 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1989:187102 CAPLUS
DN 110:187102
TI Regulatory elements involved in the bidirectional activity of an immunoglobulin promoter
AU Doyen, Noelle; Dreyfus, Marc; Rougeon, Francois
CS Dep. Immunol., Inst. Pasteur, Paris, 75724, Fr.
SO Nucleic Acids Research (1989), 17(5), 1977-87
CODEN: NARHAD; ISSN: 0305-1048
DT Journal
LA English
AB The promoter from the mouse VH441 heavy-chain immunoglobulin gene, when present on plasmids transiently introduced into myeloma cells, promotes transcription bidirectionally, due to the presence on both strands of TATA-like sequences bracketting the highly conserved decanucleotide element. The two ***divergent*** promoters compete for the transcriptional machinery, their relative strength ultimately reflecting the likeness of the two TATA boxes to the consensus sequence. Moreover, their relative activity is also strongly influenced by certain point mutations within the distally located heavy-chain ***enhancer*** . The bearing of these results on current concepts of promoter function is discussed.

L4 ANSWER 17 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 6
AN 89027189 EMBASE
DN 1989027189
TI .alpha.1(IV) and .alpha.2(IV) collagen genes are regulated by a ***bidirectional*** ***promoter*** and a shared ***enhancer*** .
AU Burbelo P.D.; Martin G.R.; Yamada Y.
CS Laboratory of Developmental Biology and Anomalies, National Institute of Dental Research, National Institutes of Health, Bethesda, MD 20892, United States
SO Proceedings of the National Academy of Sciences of the United States of America, (1988) Vol. 85, No. 24, pp. 9679-9682.
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal
FS 022 Human Genetics
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 911212
Last Updated on STN: 911212
AB Collagen IV is the major structural component of basement membranes and is a heterotrimer composed of two .alpha.1(IV) and one .alpha.2(IV) chains. Most collagen genes are dispersed in the human genome, such as the genes for collagen I, which are located on chromosomes 7 [.alpha.1(I)] and 17 [.alpha.2(I)]. In contrast, we have found that the murine .alpha.1(IV) and .alpha.2(IV) collagen genes exist in a head-to-head arrangement on ***opposite*** strands separated by 130 base pairs. By transfecting various portions of these genes into cells, we have found that transcription of the .alpha.1(IV) and .alpha.2(IV) genes is regulated by a ***bidirectional*** ***promoter*** located between the two genes working in concert with an ***enhancer*** located in the first intron of the .alpha.1(IV) chain gene.

L4 ANSWER 18 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 7
AN 88115466 EMBASE
DN 1988115466
TI The ***enhancer*** elements and GGGCGG boxes of SV40 provide similar functions in bidirectionally promoting transcription.
AU Hertz G.Z.; Mertz J.E.
CS McArdle Laboratory for Cancer Research, University of Wisconsin, Madison, WI 53706, United States
SO Virology, (1988) Vol. 163, No. 2, pp. 579-590.
ISSN: 0042-6822 CODEN: VIRLAX
CY United States
DT Journal
FS 016 Cancer
022 Human Genetics
047 Virology
LA English
SL English
ED Entered STN: 911211
Last Updated on STN: 911211
AB The early and the late genes of simian virus 40 (SV40) are transcribed in ***opposite*** directions from a shared promoter region. The 72- and the 21-bp repeat regions of the SV40 genome contain the transcriptional ***enhancer*** and six copies of the Sp1-binding GGGCGG box, respectively. SV40 mutants lacking various parts of these regions were examined in COS cells to determine the importance of these sequences for transcription in each direction. We made the following observations. (i) The 72-bp repeat region was required for efficient transcription of both the early and the late genes. (ii) The 21-bp repeat region was required for efficient early-gene transcription, but not for efficient late-gene transcription; however, it was able to supply some late-promoter activity when the 72-bp repeat region was missing. (iii) The ability of either of these regions to promote transcription was gradually reduced as the number of promoter elements within each was decreased. (iv) Mutations in these regions always decreased early-gene transcription more than late-gene transcription. These results indicate that both regions are made up of multiple ***bidirectional*** ***promoter*** elements, but that the 72-bp repeat region is more effective at inducing transcription than the 21-bp repeat region. Since each region can also (i) satisfy a need for promoter elements in the replication of viral DNA and (ii) induce a region of open chromatin, we conclude that the promoter elements within the ***enhancer*** and the GGGCGG boxes probably provide similar functions.

L4 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1987:114483 CAPLUS
DN 106:114483
TI Bidirectional activity of the rat insulin II 5'-flanking region in transgenic mice
AU Efrat, Shimon; Hanahan, Douglas
CS Cold Spring Harbor Lab., Cold Spring Harbor, NY, 11724, USA
SO Molecular and Cellular Biology (1987), 7(1), 192-8
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB A new transcription initiation site was identified in the 5'-flanking regulatory region of the rat insulin [9004-10-8] isoform II gene. This site is located on the ***opposite*** strand with respect to the insulin gene promoter, upstream of the insulin gene transcriptional ***enhancer*** . The cell-specific activity of this reverse promoter element is demonstrated in 2 lineages of transgenic mice, in which it directs expression of simian virus 40 T-antigen specifically to the .beta. cells of the endocrine pancreas, resulting in development of pancreatic tumors. Anal. of RNA from the tumor cells demonstrates bidirectional transcription from the insulin regulatory region of the transgene. These data raise the possibility that bidirectional activity is a quality of the regulatory region of the insulin gene in its natural genomic context.

L4 ANSWER 20 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 8
AN 1987:125695 BIOSIS
DN PREV198783064756; BA83:64756
TI THE MES-1 MURINE ***ENHANCER*** ELEMENT IS CLOSELY ASSOCIATED WITH THE HETEROGENEOUS 5' ENDS OF TWO ***DIVERGENT*** TRANSCRIPTION UNITS.
AU WILLIAMS T J [Reprint author]; FRIED M
CS IMPERIAL CANCER RES FUND, LINCOLN'S INN FIELDS, LONDON, WC1A 3PX, UK
SO Molecular and Cellular Biology, (1986) Vol. 6, No. 12, pp. 4558-4569.
CODEN: MCEBD4. ISSN: 0270-7306.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 7 Mar 1987
Last Updated on STN: 7 Mar 1987
AB The location in the mouse genome of the 149-base pair MES-1 element, previously isolated by its ability to restore expression to an enhancerless selectable gene, was analyzed. The active moiety of the single-copy MES-1 element is located between the 5' ends of two ***divergent*** transcription units, SURF-1 and SURF-2, both of which specify more than one mRNA species by differential splicing. The heterogenous 5' ends of the SURF transcripts are separated by only 50 to 75 base pairs, and this sequence possesses a high G+C content (65%) and contains neither the TATA and CAAT box motifs normally associated with many highly expressed genes nor the GC box motif (Sp1-binding site) associated with a number of housekeeping genes. Although MES-1 appears to have enhancerlike properties when linked to heterologous genes, its normal genomic location suggests that it functions as a ***bidirectional*** ***promoter*** . Thus, MES-1 may represent a new class of ***enhancer*** -promoter element.

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